REMARKS

Claims 1 and 3-8 are pending in the instant application. Claims 1 and 3-8 have been rejected. Claims 1 and 3-8 have been canceled. Claims 11-18 have been added. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Rejection of Claims Under 35 U.S.C. §112

Claims 1 and 3-8 have been rejected under 35 U.S.C. 112, first paragraph, as failing to meet the written description requirement. It is suggested that the claims and specification fail to provide adequate written description for the genera of claimed inhibitory agents. It is suggested that the specification does not provide a core structure of inhibitory agents and that because the prior art, as evidenced by Joshi et al. ((2002) *J. Virol.* 76:6545-6557), suggests a lack of homology in agents that bind with high affinity to the reverse transcriptase region of HIV-1, Applicants have not shown possession of the entire claimed genus of inhibitory agents. Applicants respectfully traverse this rejection.

As described at pages 1 and 2 of the instant specification, HIV reverse transcriptase is a multi-functional enzyme having RNA- and DNA-dependent DNA polymerase activity as well as a ribonuclease H (RNase H) activity. These activities enable the enzyme to reverse transcribe viral RNA to double-stranded DNA, wherein the RNase H activity cleaves the RNA portion of a DNA/RNA heteroduplex intermediate, thereby permitting the viral DNA to disengage and invade the host cell's genetic material. Accordingly, in so far as Joshi et al. teach inhibitors that

compete with the template-primer thereby blocking the *reverse-transcriptase function* of HIV reverse transcriptase (see the abstract), the teachings of Joshi et al. are not relevant to the nature of agents which bind to the RNase H domain of retroid virus reverse transcriptase and inhibit the *RNase H activity* of the enzyme.

Compliance with written description requirement of 35 U.S.C. 112, first paragraph, may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. For some biomolecules, examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length. Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession. See MPEP §2163.

Applicants respectfully disagree with the Examiner's suggestion that a core structure of inhibitory agents has not been provided. As set forth in the claims and demonstrated at pages 14-17, loops (*i.e.*, Y_1 and Y_2 of Formula I) composed of ribonucleic acid or 2',5'-linked ribonucleic acid effectively inhibit RNase H activity, whereas DNA loops are not able to inhibit RNase H activity. Furthermore, this passage teaches multiple examples of sequences, lengths, and base compositions which can make up the stem (*i.e.*, X_1 and X_2 of Formula I) of the instant composition. Moreover, pages 20-23 of the specification provide additional examples of sequences, lengths, and base

compositions which can make up the stem and, in particular, clearly disclose that the 5′-UUYG-3′/2′ loop sequence, as claimed, is essential to the recognition and binding of the RNase H domain to the inhibitory agent. In this regard, Applicants demonstrate that mutating the loop region sequence of UUCG to UACG completely abolishes activity. See page 22, lines 25-27. In particular, Applicants describe that the combination of the loop sequence and stem structure are respectively required for recognition/binding and grasping/positioning of the inhibitory agent in the RNase H domain. See page 23, lines 1-9.

Accordingly, Applicants have clearly conveyed a core sequence (*i.e.*, the 5′-UUYG-3′/2′ loop sequence of Y_1 and Y_2) and structure (*i.e.*, a stem-loop structure composed of X_1, X_2, Y_1 and Y_2 as set forth in claim 1) which are required for recognition, binding, and positioning of an inhibitory agent of the invention at the RNase H domain of a retroid virus reverse transcriptase. Moreover, Applicants have provided multiple species of the claimed genus which demonstrate that Applicants were in possession of the claimed invention at the time of filing the present application. As such, the written description requirement under 35 U.S.C. 112, first paragraph, has been met. It is therefore respectfully requested that this rejection be reconsidered and withdrawn.

II. Rejection of Claims Under 35 U.S.C. §103

The rejection of claims 1 and 3-8 under 35 U.S.C. 103(a) as being unpatentable over Hannoush et al. (Document AE, PTO-1449 filed 10/4/04) in view of Denisov et al. ((2001) *Nucl. Acids Res.* 29:4284-4293) has been withdrawn.

However, claims 1 and 3-8 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Wasner et al. in view of Hannoush et al. and in further view of Ray et al. ((2000) *FASEB J.* 14:1041-1060) for the reasons of record. Applicants respectfully disagree with this rejection.

Applicants respectfully believe that the instant composition does not flow from the teachings of the combined references. Statements such as "Ray et al. teach targeting a gene sequence using a duplex comprising a peptide nucleic acid and further teach inhibition of gene activity using a duplex comprising a peptide nucleic acid" [emphasis added](page 8 of the present Office Action) simply provide no basis for a conclusion that the skilled artisan would be motivated to combine the cited references in order to produce a ligand which binds to the RNase H domain of retroid virus reverse transcriptase and inhibits enzyme activity.

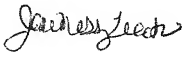
However, in an earnest effort to facilitate the prosecution of this application, Applicants have canceled claims 1 and 3-8, and added new claims 11-18 to highlight novel dumbbell compositions falling within the scope of claims 1 and 3-8, *i.e.*, compositions wherein Y_1 is 2 to 8 nucleotides in length and Y_2 is 2 to 8 nucleotides in length. While the cited references teach single hairpin structures, these references do not teach or suggest dumbbells which bind to the RNase H domain of retroid virus reverse transcriptase thereby inhibiting the RNase H activity of this enzyme. Because the cited references, when combined, fail to teach or suggest all the claim limitations (MPEP 706.02(j)) these references cannot be held to make the present invention obvious under 35 U.S.C. 103(a). It is therefore

respectfully requested that this rejection be reconsidered and withdrawn.

III. Conclusion

The Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,



Jane Massey Licata
Registration No. 32,257

Date: **January 18, 2007**

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, New Jersey 08053

(856) 810-1515